Use of the Artificial Kidney

Its Place in the Treatment of Acute Renal Failure

PETER F. SALISBURY, *M.D., Ph.D.*, Burbank

• **Of 57 patients with severe, but potentially reversible, acute renal failure who were observed during a recent four-year period, some had dialysis with an artificial kidney and some did not.**

Twenty survived with the standard "conservative" management alone; 19 survived with a combination of "conservative" and "intensive" (that is, artificial kidney) treatment; 18 patients died.

One error that was made in the management of all 18 patients who died, was excessive delay in the use of the artificial kidney.

Hemodialysis should be used whenever serious electrolyte abnormality exists, whenever the blood urea nitrogen exceeds 150 mg. per 100 cc. or whenever clinical signs of uremia first appear. One or more of these indications will usually, but not always, become evident between the fifth and the eighth day of virtual anuria.

IN RECENT YEARS there has been no major controversy or innovation concerning the "conservative" management of patients with acute renal failure; the treatment of such patients during the early stages of anuria-oliguria is now a matter of universal agreement.[3,5,7,9] It is all the more surprising to find widespread divergence of opinion regarding the more intensive modalities of treatment. While the therapeutic efficiency of the artificial kidney procedure is today widely recognized and the technique of using it has become routine in many centers, controversy about the indications for hemodialysis in individual cases is the most formidable remaining obstacle in the path toward standardized management of acute anuria. While some investigators[5] decline to publish their criteria for use of dialysis, others advocate dialysis as a routine to be employed on the fifth, sixth (3) or seventh (6) day of anuria; and still others would use it only in patients with blood urea nitrogen over 200 mg. per 100 cc.[2] The Swedish school which in the past restricted use of the artificial kidney to comatose uremic patients, intends to use it more extensively in the future. Kolff[4] is now guided by the clinical condition of the patient but has not published the particular clinical signs which he uses as signals in this respect. In earlier publications he advocated dialysis of patients with a serum potassium of 7.0 mEq. per liter or more, with carbon dioxide content of 12 mEq. per liter or less, with blood urea nitrogen of 150 mg. or more per 100 cc.

The present report concerns 57 patients with potentially reversible acute renal failure and no other associated fatal primary pathologic condition. Thirty-nine of the patients survived and eighteen died.

CLINICAL MATERIAL AND METHODS

The patients were dealt with in a four-year period ending early in 1958. In many instances I was not in charge of the clinical management and my services were confined to consultations or hemodialysis. In the case of the patients whose treatment I did manage, standard conservative measures were employed: Particular attention was directed to water balance (fluid intake usually restricted to the visible output plus 500 cc. per 24 hours), to electrolyte balance, to administration of a high caloric protein-free regimen and careful clinical and chemical supervision. Hemodialysis was performed with the portable Skeggs-Leonards machine at various hospitals in Southern California. Blood was usually withdrawn and administered via a double lumen catheter inserted into the inferior or superior vena cava by way of a saphenous or external jugular vein. Hemodialysis usually lasted about four hours and required 150 mg. of heparin in the average patient.

Presented before the Section on Urology at the 87th Annual Session of the California Medical Association, Los Angeles, April 27 to 30, 1958.

RESULTS

Itemized clinical data concerning 51 of the 57 cases presented here have been published elsewhere.[8]

1. Patients who recovered from acute renal failure without dialysis

Twenty patients recovered from acute renal failure without dialysis. Anuria-oliguria (urine output less than 500 cc. per day) continued, in this group, for from three to eleven days, the highest blood urea nitrogen was 195 mg. per 100 cc., the highest serum potassium 9.2 mEq. per liter. Severe neurological abnormality (coma) was present in three patients. Many patients had nausea and vomiting which precluded feedings by mouth or by indwelling gastric tube. Pulmonary edema or other signs of

severe cardiac decompensation were observed in three patients. Peripheral edema was observed in six instances and was always associated with excessive administration of fluid.

2. Patients who recovered from acute renal failure with the aid of the artificial kidney

In 16 of this group of 19 patients the use of the artificial kidney was considered lifesaving by all physicians concerned. In the remaining three instances the treatment was considered helpful, but one or more physicians felt that the patients might have survived without it. Anuria-oliguria continued for from eight to thirty-nine days. Hemodialysis was used as early as the fifth day and as late as the twenty-third day after the onset of anuria. In four patients dialysis was done twice. The highest serum potassium was 10.2 mEq. per liter, the highest non-protein nitrogen content was 280 mg. per 100 cc., and the highest blood urea nitrogen 240 mg. per 100 cc. Apart from the chemical indications, clinical indications for dialysis were: Severe neurological abnormality (coma, convulsions, severe twitching) in eight cases; coexistence of neurological and circulatory abnormalities (usually pulmonary edema) in seven. Previous overhydration and other earlier deviations from standard management were corrected with hemodialysis in six instances. Severe electrolyte abnormality (usually acidosis or hyperkalemia) was the primary indication for hemodialysis in eight cases and clinical manifestations of uremia were the primary indications in eleven.

The effect of the artificial kidney procedure was attested by chemical determinations and by clinical changes. Abnormal blood electrolyte levels, including abnormal blood pH, were corrected in every instance. The amounts of urea removed from the patient and recovered in the dialysis fluid varied from 38 to 180 grams. Blood urea nitrogen levels and non-protein nitrogen decreased significantly in all cases, but the decreases did not always reflect the large amount of nitrogenous material recovered in the dialysis fluid. The average change of blood urea nitrogen was from 181 mg. per 100 cc. before dialysis to 73 mg. after; the maximum change was from 160 mg. to 35 mg.; the minimum change was from 92 mg. to 52 mg. In several patients who were overhydrated the use of the portable Skeggs-Leonards artificial kidney permitted removal of fluid by ultrafiltration. As much as 4,500 cc. of fluid was removed in this manner and this "ultrafiltration" effect was considered decisive for the patient's recovery in three instances.

The effect of the artificial kidney procedure on the clinical signs and symptoms in the surviving group of patients was striking. Improvement in the patients' nervous and mental states was noticeable at intervals of time which varied from 30 minutes after the start of the procedure to 24 hours after it was finished. Most patients rested quietly during the procedure and felt decidedly improved afterward—anxiety and restlessness disappeared, twitching usually diminished, awakening from coma and stupor was common. Confusion usually, but not always, gave way to full orientation and ratiocination. In three cases dialysis was carried out despite hemorrhagic phenomena; this condition did not appear to be aggravated by the artificial kidney procedure and it ceased shortly after dialysis was finished.

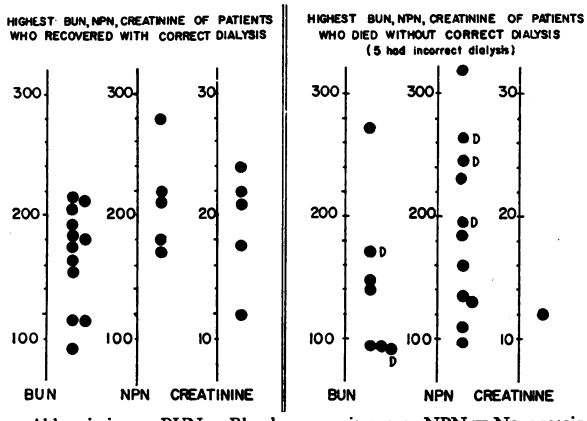
In the group of patients reported upon here, untoward incidents did not occur during dialysis. Fluctuations of the arterial pressure were observed during the procedure in about 50 per cent of the treated patients but could be readily controlled with small doses of pressor or depressor agents. Decreases of the arterial pressure usually occurred at the beginning of dialysis and were attributed to the rapid infusion of citrated priming blood; and rises of the arterial pressure were occasionally observed later during the dialysis. These fluctuations did not call for an interruption of the procedure. In one case refractory hypotension occurred during the dialysis. It was traced to the commercially available "anhydrous" calcium chloride, which contained more than 50 per cent water, and the dialysing solution made with it had caused hypocalcemia in the patient, who died nine days after the first dialysis.*

3. Patients with acute, reversible renal disease who might have survived with more appropriate therapy

When patients survive after an episode of acute renal failure it is not easy to take issue with the therapeutic management. On the other hand, the question must be posed: What went wrong when patients do not survive such episodes, when autopsy findings (available in the 18 cases reported here) show that the patients were suffering from potentially reversible lesions of the kidney and when death cannot be fairly ascribed to associated primary disease.

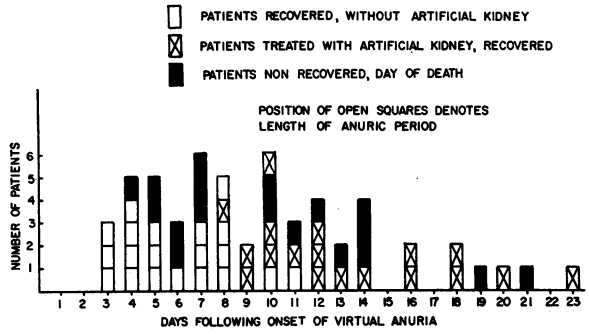
In the 18 patients with acute renal failure who died, death occurred as early as four days and as late as 21 days after the onset of virtual anuria. Three of the six "early" deaths (within seven days

*It must be said, in all fairness, that death occurred in three other patients while they were undergoing dialysis; these patients are not included in the present series (no autopsy in two, chronic disease in one). One of the patients who died during dialysis was 78 years of age and died suddenly (perhaps of embolism or cerebrovascular accident) while having dialysis on the 18th day following repair of a large aneurysm of the abdominal aorta and subsequent anuria. The other two patients had severe polycystic kidney disease, were in severe cardiac failure, and had received digitalis bodies. It is assumed that digitalis toxicity supervened in these two because of changes in electrolyte patterns during dialysis. One of the latter two developed ventricular tachycardia before dialysis began. Digitalization must be considered a definite hazard in patients who are to have dialysis.



Abbreviations: BUN = Blood urea nitrogen; NPN = Nonprotein nitrogen. The letter "D" beside some of the dots indicates use of dialysis in desperation even though it could not be expected to benefit.

Chart 1.—Comparison of highest nonprotein nitrogen, blood urea nitrogen and creatinine of patients recovered with correct dialysis and of patients who died without correct dialysis. This chart should indicate that the patients who recovered with correct dialysis were fully as sick as the patients who did not recover.



In one case (not shown on chart) the patient was uremic but not anuric.

Chart 2.—Length of anuric period in patients who recovered with or without dialysis and in patients who did not recover. This chart indicates that death can occur early or late after the onset of anuria.

of onset of anuria) could be attributable to overhydration which had resulted in pulmonary edema. In four of the "early" deaths the serum potassium was elevated above 7.0 mEq. per liter. In one "early" death, unrecognized active rheumatic carditis coexisted with the acute uremia; in this patient dialysis was done once and probably should have been repeated. There is very little doubt that more timely use of the artificial kidney would have prolonged life—perhaps until they recovered—in the patients who died "early" with hyperkalemia or from overhydration. Of the 12 patients who died eight days or more after the onset of anuria, only two had serum potassium above 7.0 mEq. per liter. Overhydration was a factor in only one of these "late" deaths. In two instances in the "late" death group the artificial kidney was applied as a measure of desperation when patients with daily urine output of 1200 and of 1800 cc. developed pulmonary edema and coma 14 and 18 days after acute tubular necrosis due to transfusion reaction. The other "late" deaths occurred presumably because repeat dialysis was not performed in time, although it should have been since these patients had been helped by earlier dialysis. In three of the "late death" patients peritoneal lavage was performed by other physicians and the artificial kidney was not employed. Six of the "late death" patients were not treated with any form of dialysis. One patient, in whom twitching began as early as the fifth day of anuria, had excellent chemical results from dialysis on the ninth day, then died, still twitching, on the twelfth day of anuria, although the serum electrolyte pattern was not abnormal a few hours before death and in spite of non-protein nitrogen of only 142 mg. per 100 cc. on the day of death.

DISCUSSION

The observations here reported on a series of 57 patients with potentially reversible renal failure uncomplicated by other serious primary disease should permit conclusions concerning the most effective use of the artificial kidney. The clinical and chemical course of acute renal failure in the group of 18 patients who died closely resembled the pattern observed in the recovered group, except for the correct use of dialysis (Chart 1). Several patients in the nonrecovered group were subject to overhydration of mild to moderate degree and to other deviations from standard management. However, similar deviations of even more striking degree occurred in some cases in the recovered group, and therefore the unfavorable outcome in the 18 cases in which the patient died cannot be attributed entirely to nonstandard conservative treatment but must also be ascribed in part to excessive delay in the use of the artificial kidney.

It has been found that the uremic syndrome due to acute renal failure evolves in a fairly well defined pattern when the patient is managed according to standard principles. Such patients will frequently be asymptomatic or have only mild signs (nausea, abdominal distention) for periods ranging from five to twelve days. As the uremia becomes more intense, relatively slight nervous signs (reflex hyperactivity, restlessness, confusion, drowsiness) or circulatory signs (loud P_2, low diastolic pressure, expiratory wheezes) will appear. Death due to circulatory failure may occur within 24 hours, and usually within three or four days, of the first appearance of two or more of the clinical signs of uremia mentioned above.

In the present series there were 14 patients with hyperkalemia (serum potassium in excess of 7.0 mEq. per liter) (Table 1). Three of these patients

TABLE 1.—*Hyperkalemia as a Cause of Death*

(Serum potassium above 7.0 mEq. per liter)

Number of patients	14
Survived without dialysis	3
Survived with dialysis	5
Died, dialysis not used	6

TABLE 2.—*Patients with Anuria-Oliguria of Seven Days or Less*

Survived without dialysis	14
Survived with dialysis	0
Died without dialysis	6
Died with dialysis*	1

*Patient had acute rheumatic carditis as well as acute renal failure.

survived with "conservative" management, five survived with a combination of "conservative" and artificial kidney treatment, and six died. Of the six hyperkalemic patients who did not survive, none had the benefit of timely artificial kidney therapy. Hyperkalemia must therefore be considered as an indication for hemodialysis even though it is possible that some patients with a high serum potassium may recover without the use of the artificial kidney.

In the present series death from acute renal failure occurred as early as the fourth day and as late as the twenty-first day after the onset of virtual anuria (Chart 2). During the later stages of acute renal failure, when the serum electrolytes may be normal and diuresis may already have set in, death may still occur and can be preceded by only a short premonitory period during which signs and symptoms of uremia are observable (Tables 2, 3 and 4). Although patients in the terminal stage of uremia (coma, convulsion, pulmonary edema) have often been rescued by the artificial kidney, it is now agreed that hemodialysis should be employed earlier, not only because it prevents the development of irreversible complications, but also because the fatal progress of the disease is often too rapid to permit the start of intensive treatment when there has been excessive delay. Although 14 patients survived periods of anuria of seven days or less without dialysis, six patients died during the first seven days of anuria when their lives presumably could have been saved by the artificial kidney treatment. Although six patients survived more prolonged anuria without dialysis, and 19 survived with dialysis, eleven such patients died because they either did not receive dialysis treatment or received it only as a measure of desperation.

Ideally, therefore, the proper indications for artificial kidney treatment are as shown in Table 5. These indications require repeated daily reevaluation of the patient. Physicians who seldom see a patient with acute anuria will find it difficult to supervise anuric patients carefully enough. It has therefore been recommended that the first dialysis of anuric patients should be considered on the fifth or sixth day of anuria.[4] If the 57 patients described here had been managed according to this rule, most of the 18 patients who died would have had hemodialysis in time and would probably have survived, whereas only six patients in the series would have been treated with the artificial kidney without need.

TABLE 3.—*Patients with Anuria-Oliguria Eight Days or More*

Survived without dialysis	6
Survived with dialysis (1 patient with acute uremia, without oliguria)	19
Died without dialysis*	11
Died with correctly employed dialysis	0

*Dialysis was used as a measure of desperation or otherwise incorrectly in five of these cases.

TABLE 4.—*Probable Mechanism of Death in Patients Who Died from Acute, Reversible Renal Failure*

Death occuring on or before 7th day of oliguria:	
Hyperkalemia	3
Overhydration	3
Failure to use artificial kidney in time	6
Death occurring on or after 8th day of oliguria:	
Overhydration	1
Electrolyte abnormality (potassium, pH)	2
Coma, convulsions	8
Tachycardia, pulmonary edema	6
Failure to use artificial kidney in time	12

TABLE 5.—*Indications for the Use of the Artificial Kidney*

I. Chemical indications:
   (a) Serum potassium 7.0 mEq. per liter or more.
   (b) Rapidly mounting serum potassium.
   (c) Carbon dioxide 12. mEq. per liter or less.
   (d) Blood urea nitrogen 150 mg. per 100 cc. or nonprotein nitrogen 200 mg. per 100 cc.

II. Existence of two or more of the early clinical signs of uremia (reflex hyperactivity, restlessness, confusion, drowsiness, loud P_2, low diastolic pressure, expiratory wheezes).

III. If, after dialysis, the above indications recur, dialysis should be repeated in compliance with the above indications, even though diuresis may already have set in.

St. Joseph Hospital, Burbank.

REFERENCES

1. Alwall, N., Erlanson, P., Nyman, M., and Tornberg, A.: On the artificial kidney, Acta Med. Scand., XXIX:152-353, 1955.

2. Anthonisen, P., Brun, C., Crone, C., Lassen, N. A., Munkend, O., and Thomsen, C.: Clinical experience with the Skeggs-Leonards type of artificial kidney, Lancet II:1277, Dec. 22, 1956.

3. Elkinton, J. R., and Danowski, T. S.: The Body Fluids, Williams and Wilkins, Baltimore, 1955, p. 561.

4. Kolff, W. J.: The artificial kidney, past, present and future, Trans. Am. Soc. Artf. Int. Org., 1:1-8, 1955.

5. Merrill, J. P.: The Treatment of Renal Failure, Grune and Stratton, New York, 1955.

6. Murphy, F. D. (Milwaukee): Personal communications, 1957.

7. Relman, A.: Diagnosis and management of renal failure, Disease of the Month, June 1956.

8. Salisbury, P. F.: Timely versus delayed use of the artificial kidney, Arch. Int. Med., 101:690, 1958.

9. Strauss, M. D., and Raisz, L. G.: Clinical Management of Renal Failure, Thomas, Springfield, 1956.